Topographic organization of the human secondary somatosensory cortex: A combined MEG-fMRI study

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1 Introduction

Functional Magnetic Resonance Imaging (fMRI) allows to localize an event-related increase of metabolism due to neuronal firing in active brain regions as reflected by blood flow and oxygen consumption, during perception and processing of a sensory impulse from a given body district [1]. Magnetoencephalography (MEG), on the other hand, by localizing in 3D the sources of the associated magnetic field, directly investigates event-related cerebral activity with millisecond time resolution [2]. In contrast, fMRI has a temporal resolution in the order of 1 s, being limited by hemodynamics. There is an increasing interest in the scientific community for the combination and comparison of brain mapping techniques with complementary properties [3].

The Secondary Somatosensory Area (SII) is a center that receives sensory inputs from both sides of the body and is located near the primary auditory cortex [4]. In humans, activation of SII area has been observed during median and tibial nerve stimulation by means of magnetoencephalographic recordings indicating sources in bilateral areas adjacent to the Sylvian fissure [5]. With fMRI, SII has been observed to activate bilaterally upon tactile stimulation of the hand [6]. The SII area contains different representations of different body districts such as upper and lower limb, and face, as it has been observed in former [7], and in more recent [8] MEG recordings. Recently, we have demonstrated a roughly somatotopic organization of SII by means of fMRI and electrical stimulation of the upper and lower limb [9].

In this work, we compared fMRI activations, and Equivalent Current Dipole (ECD) localizations from evoked MEG data, following median and tibial nerve stimulation.

2 Methods

Five neurologically healthy volunteers were enrolled after having obtained their signed consent and the approval of the local Ethics Committee (four males, one female, mean age 26 years). All of them were right handed.

2.1 Stimulation procedures

Stimuli were electric rectangular pulses, 0.2 msec in duration, except in one subject where the duration was raised to 0.4 msec in order to reach the motor threshold. The repetition rate was 0.3 Hz for MEG and 1.9 Hz for fMRI. Usually, a lower repetition rate is chosen since a short inter-stimulus interval has been seen to reduce the SII response. A higher stimulation rate was chosen here for fMRI, because regional cerebral blood flow has been seen to increase with stimulus rate [10]. Stimuli were unilaterally delivered to right or left median nerve at the wrist or to the tibial nerve at the medial malleolus. No artifacts due to the stimulating apparatus were visible in the raw functional MR images. Intensities of stimulation were settled at a level producing a painless, clearly visible thumb opposition or foot flexion. Stimuli were delivered by means of a pair of non magnetic, 3 cm spaced, Cu-Sn disk electrodes filled with conductive jelly (skin-electrode resistance < 5 kΩ), via a twisted and shielded pair of wires.

2.2 fMRI

MRI scans were carried out via a Siemens Magnetom Vision 1.5 Tesla scanner with echo-planar imaging capability. Functional imaging volumes consisted of 20 to 22 – depending on subject anatomy – bicommissural transaxial slices, 3 mm in thickness with no gap, a 128 x 128 matrix, a field of view (FOV) of 250 mm. Volumes covered the upper part of the brain from the head vertex to – and including – the upper bank of the temporal lobes. FMRI sequences were of the Echo Planar Imaging (EPI) Free Induction Decay (FID) type with a Time Relaxation (TR) of 0.8 msec and a Time Echo (TE) of 54 msec, flip angle of 90 degrees. Functional imaging volumes were acquired according to a block paradigm where a group of ten volumes of the stimulus condition was alternated with a group of ten volumes of the control condition. In total, three groups of ten volumes for each condition were acquired. The scan time for each volume was 2 seconds, while a 3 second interval separated the starting of two consecutive volumes. A high-resolution whole brain structural image (FOV of 250 x 250, 256 x 256 matrix, 1 mm slice thickness with no gap, voxel size 0.9766 mm x 0.9766 mm x 1 mm, flip angle 12°, TR = 9.7 msec, TE = 4 msec) was acquired via a 3D MPRAGE (magnetization prepared rapid gradient echo) sequence.

Analysis of fMR images was performed using MEDx software package (Sensor Systems [11]). After correction of motion artifacts, statistical brain activation images were generated by a Student t-test comparing, voxel-by-voxel, images of the stimulus condition to those of the control condition; thereafter, Z-score activation maps were obtained. Activated voxels were selected by means of a clustering algorithm; the statistical significance of activated voxels was assessed on the basis of their Z-score value and of the presence of other nearby activated voxels. Finally, the clustered Z-score maps were transformed into the Talairach coordinate space [12], and superimposed on the high resolution, Talairach transformed, anatomical images.

2.3 MEG

Magnetic field recordings were performed with the whole head system operating at the University of Chieti [13]. This system is equipped with 165 integrated SQUID magneto-meters, 153 of which are distributed over the helmet shaped dewar bottom, and 12 of which are arranged into orthogonal triplets located in the upper part of the dewar, and used as references for software noise compensation. MEG data were acquired at 1 kHz sampling rate and bandpass filtered at 0.16 – 250 Hz. About 150 trials were averaged in time to obtain 400 ms epochs starting at stimulus presentation.

Before and after MEG recordings the signal of current carrying coils placed on the subject head was recorded, and the coils subsequently localized in order to find the dewar position during measurements. Landmarks on the head of the subjects, and the positioning coils were digitized by means of a 3D digitizer (Polhemus) in order to define the subject reference system, and to locate the dewar with respect to it. Part of the digitized landmarks were also identified in the structural high resolution MRI described above, by means of 7 mm diameter spherical oil capsules, applied over the landmarks.

Data were analyzed using the Equivalent Current Dipole (ECD) as the source model, and the homogeneous sphere as the head model. The sphere was fitted to the brain surface as obtained from MRI. The ECD parameters were estimated by a least-squares fitting algorithm, where the forward solution took into account the effect of volume currents [14]. ECD location was then transformed to the reference frame of MRI, and subsequently transformed to Talairach space. Finally the ECD were superimposed on the structural, Talairach transformed MRI. This last transformation allowed the comparison between ECD location and the fMRI activations.

3 Results

3.1 fMRI

Bilaterally activated areas were observed in the supratemporal regions corresponding to the SII cortices. Median and tibial nerve activation maps, superimposed on structural high resolution images, disclosed a rough but clear somatotopic organization. In most hemispheres, a clearcut separation between the medial and tibial areas was observed - the median nerve being more anterior and more inferior than the tibial nerve-, while in a few cases they partially overlapped. On the other hand, no difference in extension and location in the medial-lateral direction was observed between median and tibial nerve areas. Differences due to stimulated side were then examined by superimposing activation maps, obtained from left and right stimulation, to the high resolution structural images. Various spatial relationships between left stimulation and right stimulation activations were observed ranging from complete separation to almost complete overlapping, with only very small regions being activated exclusively by right, or exclusively by left side stimulation, the most frequent case being partial overlapping.

3.2 MEG

For median and tibial nerve stimulation, dipolar activity was observed on MEG maps in the parietal area, contralaterally to the stimulated side, and in the parieto-fronto-temporal area, bilaterally. Maximum intensities of the extrema of the field distributions were observed in the contralateral parietal area, consistent with SI, at early latencies around 20 ms for median, and 40 ms for tibial nerve, respectively. Later components were observed bilaterally, with a latency ranging between 100 and 160 ms both for median and tibial nerves.

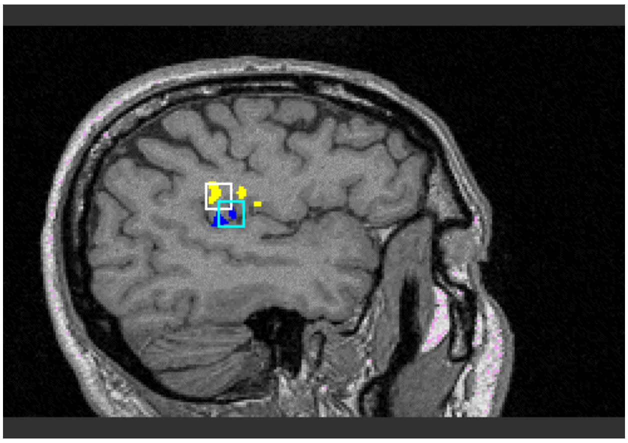

Figure 1: *Subj. GLRO. Left limb stimulation, right hemisphere. FMRI activations: Blue = median nerve; Yellow = tibial nerve; ECDs boxes: Cyan = median nerve; White = tibial nerve.*

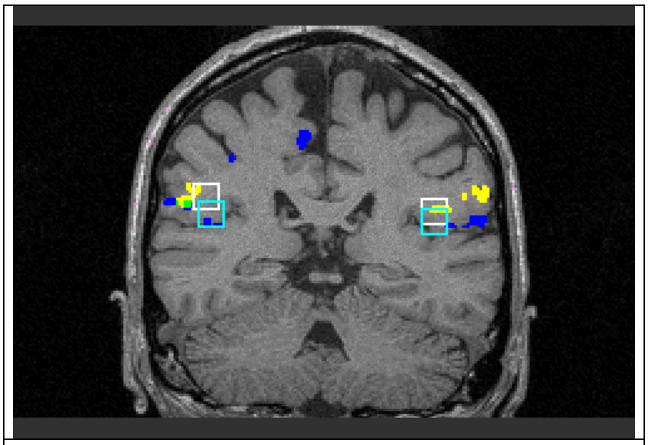

Figure 2: *Subj. GLRO, left limb stimulation. Right hemisphere is on the left. See legend of Figure1.*

Stable ECD localizations corresponding to these later components were found bilaterally near the posterior Sylvian fissure, corresponding presumably to the SII cortices. ECDs for median and tibial nerve showed different localizations suggesting a somatotopic organization of SII.

Comparison of ECD localizations and fMRI activations showed substantial consistency (see figure 1). However slight differences in localization were observed. Indeed, the mean distance between ECD position, and the position of the most significant cluster of activation across all stimulated limbs and all hemispheres, was about 9 mm in Talairach space, ranging from 6 to 13 mm.

4 Discussion

Bilateral responses are due both to parallel projections and serial activation via cortico-cortical, transcallosal fibers. Our fMRI findings show a consistent segregation of activated voxels for upper and lower limb nerves, speaking in favor of a topographical organization of SII, with the lower limb located more posterior, rostral and medial than the upper limb.

FMRI findings on the SII cortex were confirmed in most subjects by MEG recordings analyzed with the ECD model. In particular, a somatotopic organization was suggested by the mutual spatial relationship between ECDs, consistent with that already observed in a large number of subjects in a recent study with MEG only [8]. One of the subjects showed a spatial organization reversed with respect to the average. This mismatch may be due to large between subject variability due to the complicated anatomy of this cerebral area. A mismatch in localization between ECDs and fMRI activations was observed. The Euclidean distance between the ECD location and the most significant cluster of fMRI activation was calculated for all stimulations and hemispheres. This figure ranged between 6 and 13 mm, with a mean value across all stimulations and hemispheres of about 9 mm. The latter figure is somewhat smaller than what is usually indicated in the literature. Part of this mismatch could be due to co-registration errors between MEG and structural MRI. However there is no reason to assume that ECD should exactly coincide with fMRI activations. On average, the ECD locations were deeper than the corresponding fMRI activations (see figure 2). This is consistent with the insensitivity of MEG to possible radial sources located more superficially on the gyri.

The present investigation emphasizes the usefulness of a combined approach to brain function by MEG and fMRI which elucidate different aspects of brain activation, and provide a complete and anatomically detailed view of a distributed network with an extremely high time resolution.

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